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10/529,748	03/30/2005	Berislav V Zlokovic	GRT/4061-32	1588

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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER

KOLKER, DANIEL E

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1649

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/529,748	Applicant(s) ZLOKOVIC ET AL.	
	Examiner Daniel E. Kolker	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6,13,16-18,25,29,30 and 34-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6,13,16-18,25,29-30,34-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. The remarks filed 30 June 2010 have been entered. No claim amendments were submitted; claims 6, 13, 16-18, 25, 29-30, and 34-38 are pending and under examination.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 13, 16-18, 25, 29-30, and 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bertilsson (U.S. Patent Application Publication 2003/0165485) in view of Hung (U.S. Patent Application Publication 2003/0060415).

This rejection stands for the reasons previously made of record and explained in further detail below. Before turning to the rejection itself and applicant's arguments, it is important to note the breadth of the claims. The claims are drawn to methods comprising administering human protein S (each of independent claims 6, 25, and 30) to human patients who have suffered a stroke (claims 6 and 30, note cerebral ischemia recited in claim 6 is a form of stroke) or neurotrauma (claim 25, which is broad but clearly includes stroke, as stroke leads to trauma for neurons). The claims require only a single step, namely administering "an effective amount of human protein S" to the relevant patients. Certain claims (claim 6 and those claim which depend from it) are drawn to a "method of protecting" cells including neurons, but those claims involve the same single step, namely administering human protein S to patients who have had one of the recited diseases or conditions. Other claims do not recite a cellular mechanism, they

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are drawn simply to "treating neurotrauma" (claim 25) or "treating stroke" (claim 30) by administering human protein S.

Bertilsson teaches treating stroke in human patients by administering protein S; see for example paragraph [0016] for teaching that protein S is to be used for treating "a disease or disorder of the central nervous system in a mammal in need of such treatment". CNS diseases to be treated include ischemic disorders such as stroke, as well as trauma (see paragraph [0139], in particular the sentence bridging pp. 14-15. While mammals in general are to be treated, humans in particular are taught by Bertilsson as appropriate subjects; see paragraph [0140]. Bertilsson does not teach administration of protein C or activated protein C (note each of the independent claims requires that protein C or activated protein C is not administered). The only difference between independent claims 6, 25, and 30 is that Bertilsson does not explicitly require administration of human protein S, rather the document is generic and implies that any form of "protein S" can be used.

As set forth previously, Hung teaches administration of human protein S is therapeutic for human patients; see for example paragraph [0041] and claims 1 and 48 for teaching that protein S should be administered for treating certain medical conditions, as well as paragraph [0085] for teaching that human forms of the protein are preferred. However while Hung teaches treatment of ischemia of the heart (paragraphs [0011], [0019], [0023], and [0025] for example) the reference does not teach treatment of stroke or cerebral ischemia or neurotrauma as required by the independent claims.

Nevertheless, it would have been obvious to one of ordinary skill in the art to modify the teachings of Bertilsson, who teaches the step of administering protein S for treatment of stroke, by selecting human protein S taught by Hung, thereby arriving at the invention of claims 6, 25, and 30. Choosing the human form of protein S would have been obvious, as it would reduce the likelihood of immune rejection of a foreign protein.

Applicant argued that the invention as claimed would not have been obvious. Specifically, in the remarks filed 30 June 2010, applicant made the following points:

- 1) There is no teaching or suggestion in Bertilsson that protein S has neuroprotective properties;
- 2) One of ordinary skill in the art would not accept Bertilsson's teaching that protein S can be substituted for Gas6, and since protein S is not functionally equivalent to Gas6 the findings on Gas6 cannot be extended to protein S;

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3) The specific experiments performed by applicant and described in the present specification were not performed by Bertilsson;

4) Agents which promote neurogenesis do not necessarily have neuroprotective properties, so the teaching that protein S promotes neurogenesis cannot be extended to claims drawn to neuroprotection;

5) Hung teaches away from the present invention.

The arguments set forth above have been fully considered but they are not persuasive. Each will be answered in turn.

With respect to 1) above, it is important to note that only one of the independent claims recites neuroprotection. Neither claim 25 nor 30 mentions this phenomenon; those claims are drawn to "treating" either neurotrauma in general or stroke in particular. Claim 6 does in fact recite "A method of protecting one or more cell types of a human subject's central nervous system". However the step recited in claim 6 is simply administering protein S, wherein no protein C or APC is administered, to a patient with brain injury caused by stroke (i.e. cerebral ischemia). The only difference between the invention of claim 6 and the disclosure of Bertilsson is that the latter teaches administration of protein S in particular and does not teach human protein S as claimed. Applicant did not argue that selection of human protein S in particular would be non-obvious, but argued that the finding of a different mechanism provides patentability. But since Bertilsson taught that the same protein (protein S) could be administered to patients with stroke, selecting human protein S in particular would be obvious, particularly as Hung teaches that the human form of the protein can be used for treating humans.

2) Applicant enters, on p. 7 of the remarks filed 30 June 2010, a detailed discussion of the minute details of Tyro3/Sky signaling which are not recited in the claims and which are not germane to the invention claimed. The argument appears to be that since Bertilsson only provided reduction to practice of Gas6-based experiments, since there was some uncertainty as to the signaling pathways one of skill in the art would not believe Bertilsson's assertions that protein S could be substituted for Gas6. This argument is not persuasive. The examiner has already cited evidence, published after the Nyberg reference cited by applicant, indicating that protein S and Tyro3 can in fact interact. One of ordinary skill in the art would have reason to believe, not doubt, the assertions of Bertilsson that experiments with Gas6 can be extended to protein S. While some details of the Tyro3/protein S signaling pathway may not have been fully

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developed by the time Bertilsson was published, the reference provides a reasonable expectation of success in treating stroke by administering protein S. While Bertilsson does not explicitly teach administering human protein S, this deficiency is cured by Hung.

3) The particular experiments described in applicant's specification may not have been performed by Bertilsson, or by anyone else for that matter. However that is not germane to the discussion of obviousness or non-obviousness of the claimed invention, as applicant is not claiming specific experiments but is claiming administration of human protein S to patients with stroke; the identical method, with the exception of the specific type of protein S to be used, was taught by Bertilsson.

4) Applicant is again arguing that discovery of a slightly different mechanism of action of an old method is deserving of patentability. Although applicant has referred to several cases in which neurogenesis occurs but neuroprotection does not, this does not suggest that selecting human protein S for treating human stroke patients is a patentable contribution when the method of administering protein S (in general) to stroke patients was already known. The recitation of protection in the preamble of claim 6 does not affect patentability, since the body of the claim sets forth an obvious variant of what was disclosed by Bertilsson.

5) Hung does not teach away from the present invention. While it is of course true that Hung teaches administration of human protein S to the pericardial space, that is not a teaching away from the present invention. That the human form of protein S is suitable for treating damage to the heart does not indicate or suggest a lack of efficacy for treating stroke. There is no teaching or suggestion in Hung that the human form of protein S will be ineffective, or even sub-optimal, for treating stroke. While Hung teaches it can be used to treat ischemic damage to the heart, the fact that the reference is silent on efficacy of the same protein for treating ischemic damage to the brain does not constitute a teaching away. See also MPEP § 2145(X)(D)(1).

For at least the reasons above, the prior art of record renders obvious the claimed invention. The reference by Bertilsson explicitly teaches administration of protein S to patients with stroke. The sole difference between the method steps as claimed and those set forth by Bertilsson is that the latter does not explicitly teach administration of human protein S. But Hung teaches administration of human protein S for ischemic damage to the heart, so it would have been obvious to one of ordinary skill in the art to modify the general teachings of Bertilsson

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by selecting the specific form of protein S taught by Hung, thereby arriving at the claimed invention.

Conclusion

3. No claim is allowed.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel E. Kolker whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Daniel E Kolker/

Primary Examiner, Art Unit 1649

August 31, 2010